a pattern typical of venereal disease, and it is well documented that human papillomavirus infection develops in two thirds of those who have intercourse with a partner who has genital warts. The mean incubation period is three months. In one study, condylomas were found in 19% of cervical biopsy specimens, and some form of dysplasia was found in 43% of the specimens with condylomas. Condylomas were present in 30% of the 146 cases with dysplasia. The mean age of patients with only dysplasia was 31 years but it was 24 years for those with dysplasia and condyloma.

Data suggesting that papillomavirus-induced cervical lesions may lead to cancer are rapidly accumulating. In an editorial recently the importance of caution in interpreting these lesions was emphasized. The authors concluded that "women bearing the virus-associated lesions should receive the same clinical and colposcopic evaluation, treatment and follow-up as usually administered to women with conventional forms of cervical intraepithelial neoplasia until more data on the natural history of these lesions are obtained."

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Tumor Markers

A MAJOR GOAL in the war on cancer is to advance the time that malignancy is first diagnosed so that effective treatment can be instituted earlier. Pathologists are aware of histologic "markers" of malignancy and note that the cellular order of cancer is less differentiated and more like fetal tissue than is the structure of normal adult tissue. It is not surprising that tumors also often produce fetal products including proteins, enzymes, hormones, serum components, cell surface glycoproteins or cytoplasmic constituents that are characteristic of less differentiated tissue. Measurement of the serum concentrations of these "oncodevelopmental" markers in selected instances has been useful for diagnosis, prognosis and determination of the effectiveness of therapy. Immune labeling of tissue sections is useful for determining the origin of certain cancer cells, and radiolabeled antibodies to tumor markers are used to locate tumors in vivo by radioimmunoscintigraphy. More recently, antibodies to tumor markers have been administered to patients for passive immunotherapy, and experimentally the effectiveness of this procedure is increased by coupling toxic molecules, such as the α-chain of ricin, to the antibody.

The first cancer marker was recognized by a British physician, McIntire, in 1846. This became known as Bence-Jones protein in honor of Dr H. Bence-Jones, who noted the association of this protein with a bone disease then known as "mollities ossium" and now called multiple myeloma. More than 100 years later, this protein, which precipitates in the urine of affected patients when the urine is heated at acid pH, was identified as an immunoglobulin light chain. During the past 20 years, many other tumor markers have been identified, such as carcinoembryonic antigen, α-fetoprotein, pancreatic oncofetal antigen, prostate-specific antigen, melanoma antigens, glial fibrillary protein and other nerve cell products as well as excess or ectopic hormone production, production of enzymes or isozymes, keratin, cytoplasmic proteins and connective tissue components. In a limited number of cases, production of a biologically active molecule such as a hormone may result in symptoms ("paraendocrine syndrome") that may call attention to the possibility of production by a tumor.

At present, a number of new markers is being identified by monoclonal antibodies. The high specificity of this generation of reagents may permit much more precise diagnosis. In addition, monoclonal antibodies may open the door to more specific immune therapy by passive transfer. In anecdotal reports such an approach has shown positive results in selected patients. Broad clinical trials are now under way.

The increasing availability of molecular probes for DNA or RNA sequences or rearrangements associated with cancer may ultimately provide new diagnostic approaches not now available. About 50% of tissues from hepatocellular carcinoma contain hepatitis B virus DNA, and several animal "oncogenes" have been identified in human cancers. It is possible that probes for such structures or for gene rearrangements may replace histologic examination as the major diagnostic tool for differentiating normal and cancerous tissue. For the foreseeable future, however, definitive cancer diagnosis depends on pathologic examination of a tissue specimen, and tumor markers remain useful adjuncts for tumor diagnosis.

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Prognostic Features and the Management of Cutaneous Malignant Melanoma

DURING THE PAST DECADE one of the major advances in the management of malignant melanoma has been the ability to distinguish two categories of patients: those unlikely to experience recurrence or spread (low-risk primary) and those with significant risk (high-risk primary).

The criteria of these two categories include both clinical and histologic factors. The most important histologic feature is tumor thickness measured in millimeters from the skin or ulcerated surface to the deepest area of invasion. Tumors less than 0.76 mm are of low risk and those greater than 1.5 mm are of high risk. Additional factors include the mitotic index, vascular invasion and microsatellites. Clinical factors must also be evaluated in assessing risk. Sex and site are major